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Physiology, Albumin

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Introduction

Albumin is the most abundant circulating protein found in plasma. It represents half of the total protein content (3.5 g/dL to 5 g/dL) of plasma in healthy human patients. Albumin is synthesized by liver hepatocytes and rapidly excreted into the bloodstream at the rate of about 10 gm to 15 gm per day. Very little albumin is stored in the liver, and most of it rapidly excretes into the bloodstream. In humans, serum albumin functions as a significant modulator of plasma oncotic pressure and a transporter of endogenous and exogenous (i.e. drugs) ligands. In clinical medicine, serum albumin can be measured via standard serum laboratory testing, and this measure has been advocated as a highly sensitive marker for an individual patient's nutritional status. [1]

Albumin is also a colloid fluid administered to patients in need of fluid resuscitation, especially in the setting of trauma (i.e. hypovolemic shock) or in the setting of large volume paracentesis. As a laboratory value, serum albumin can also aid clinician's regarding insight into patients' liver function or ability to biosynthesize proteins and factors vital to total body homeostasis. [0][0][0]

Issues of Concern

A 2017 meta-analysis investigating low levels of serum albumin in orthopedic patients suggested a 2.5-fold increased risk of surgical site infections (SSI) following various procedures. Procedures investigated included:

- Femur fracture patients (trauma patients, including femoral neck fractures)
- Total Knee Arthroplasty (TKA) and Total Hip Arthroplasty (THA) patients
- Spinal procedures (fusion, decompression, metastases cases, and spondylectomy studied groups)

Albumin levels <3.5 g/dL conferred this aforementioned risk [1].

Cellular

Human albumin is a small globular protein with a molecular weight of 66.5 kilodaltons (KDA). It consists of 585 amino acids which are organized into three repeated homologous domains and is made up of two separate sub-domains, A and B.

Organ Systems Involved

Synthesis of albumin takes place in the liver, after which it is excreted into the bloodstream. Albumin can be found in the bloodstream, interstitial space, as well as other fluids. When found in other fluids in large concentrations, such as in ascites or urine, it is often an indication of underlying pathology.

Function

Human albumin acts as the most significant modulator of plasma oncotic pressure and functions to transport a variety of substances called ligands.

Those ligands transported by serum albumin include endogenous ligands such as bilirubin, ions, fatty acids, and exogenous ligands such as drugs. The list of drugs transported by albumin includes methadone, propranolol, thiopental, furosemide, warfarin, methotrexate, alfentanil, and many others. Severe liver disease can result in hypoalbuminemia, which leads to fewer available binding sites for exogenous drugs. This results in larger amounts of the unbound exogenous drug, which can lead to increased drug sensitivity. This sensitivity manifests when patients have serum albumin concentrations lower than 2.5 g/dL.

Once albumin enters the circulation, about 30% to 40% stays in the bloodstream, and the remainder enters the interstitial space. The majority of protein that leaves the circulation then returns to circulation via the lymphatic system. The circulatory half-life of albumin is 16 hours. The majority of albumin's osmotic effect is attributed to its large molecular weight, while the rest is thought to stem from its negative charge. The latter allows albumin to attract positively charged molecules and, ultimately, water into the intravascular compartment. By influencing oncotic pressure, albumin has a major influence on capillary membrane pressure, which is represented by the equation:

- CP = (HP - HP) - r(OP - OP)

Where CP is capillary membrane pressure, HP is capillary hydrostatic pressure, HP is interstitial hydrostatic pressure, r is the reflection coefficient, OP is the capillary oncotic pressure, and OP is the interstitial oncotic pressure.

Pathophysiology

Hepatic albumin synthesis is not of high priority, and synthesis takes place when the body is nourished adequately. A poor nutritional state, inflammation, exposure to hepatotoxins, and exposure to high colloid osmotic pressure inhibit synthesis.

Clinical Significance

In clinical medicine, human serum albumin is a basic laboratory measurement and is transfused as a colloid fluid. In the laboratory, bovine serum albumin is used as a laboratory standard. [0][0][0]

Serum Albumin as a Laboratory Test

The liver's biosynthetic capacity or, in other words, a patient's liver functioning can be measured by drawing their serum albumin. Albumin is often coupled with a prothrombin time and/or international normalized ratio to more fully assess liver biosynthesis. However, serum albumin values can be normal in states of chronic liver disease and abnormal in cases of normal liver function. In a review of patients undergoing evaluation for gastric bypass, liver pathology and liver function tests correlated poorly. Further, hypoalbuminemia can reflect decreased albumin synthesis or a decrease in concentration relative to the free fluid. The latter state of hypoalbuminemia can be seen in cases of hepatic failure with ascites, as well as, renal or congestive heart failure. Thus, the patient's entire clinical context must be considered during the evaluation and diagnostic workup.

Often, patients who are malnourished have hypoalbuminemia or low serum albumin levels. The effects of fasting can have rapid onset with fasting leading to a one-third decrease in albumin within 24 to 48 hours of fasting onset. However, this reverses quickly with replenishment restoring the liver's ability to synthesize albumin within 15 to 30 minutes. Since malnourishment has been associated with adverse events in the postsurgical period, it is commonly used as a clinical measure for nutritional optimization and readiness for surgery. Albumin is one of many such laboratory measurements utilized to evaluate the nutritional status of a patient. Other laboratory measurements include pre-albumin, transferrin, and retinol-binding protein. However, none of these laboratory measurements stand alone, and they must be combined with a physical examination of the patient. Hypoalbuminemia is also useful for diagnosis and monitoring of patients with anasarca and malabsorption.

Albumin has additional utility in the diagnostic workup of patients with fluid accumulation in the peritoneum, or ascites. A patient can have ascites for a wide variety of reasons, including congestive heart failure, liver failure, and malignancy. A clinician can perform a diagnostic paracentesis to drain ascitic fluid and compare the albumin in this fluid to serum albumin levels and calculate a serum ascites-albumin gradient (SAAG).

SAAG = serum albumin - ascitic fluid albumin.

A SAAG of 1.1 or greater suggests ascites secondary to a portal hypertensive etiology such as congestive heart failure, hepatic cirrhosis, and alcoholic hepatitis. A SAAG of less than 1.1 indicates ascites of a non-portal hypertensive etiology such as peritoneal carcinomatosis, Mycobacterium tuberculosis, nephrotic syndrome, pancreatitis, and serositis.

Serum Albumin as a Colloid Fluid

The clinical use of the colloid fluid, albumin, in critically ill patients is a topic of debate. Some clinicians advocate for the use of albumin because it remains intravascular for longer than crystalloids and theoretically leads to less pulmonary edema. However, the benefits of albumin over crystalloids, for example, Lactated ringers, and normal saline have not been proven in trials. Furthermore, the clinician must consider the relatively higher cost of albumin in comparison to crystalloids. When treating hypovolemic shock, the first consideration is, "what is the patient losing?" If they are in shock secondary to hemorrhage from a gunshot wound, for example, packed red blood cells are of greatest importance. However, albumin is theoretically advantageous over crystalloids for its potential to increase a patient’s oncotic pressure. Its short half-life limits the effects of albumin.

As mentioned above, a strength albumin has over crystalloids is that it leads to an increase in intravascular oncotic pressure. There are some situations in which a patient needs improved oncotic pressure, and this characteristic can be advantageous. In cirrhotic patients receiving large volume (more than five liters) paracenteses, giving the patient 6 gm to 8 gm of albumin for each liter of ascetic fluid drained could lead to less incidence of hemodynamic compromise. However, a recent systematic review concluded that in cirrhotic patients without hepatocellular carcinoma, there is no mortality benefit to administering albumin after large volume paracentesis. More studies are needed to confirm or refute this finding.

Serum Albumin and wound complications in orthopedic surgery

Surgical site infection (SSI) is an unfortunately common postoperative complication encountered throughout the entire field of orthopedic surgery (e.g. orthopedic spine surgery, elective total joint replacement, orthopedic trauma cases). Serum albumin <3.5 g/dL has been demonsrated to confer an increased risk of SSI following these procedures. Especially in the setting of elective THA and TKA procedures, which demonstrate a wide range of reproducibility and success in regard to positive short- and long-term outcomes in the appropriately selected patients [8][9][10][11], patient malnutrition status is often given consideration when performing these procedures.

Questions

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